Off-the-Shelf Engineered iPSC-derived NK and T Cells for the Treatment of Cancer
Forward-Looking Statements

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Changing the Game in Cell Therapy

*Off-the-Shelf Cell Products to Eradicate Cancer*

**Multiplexed Engineering**
Incorporate multiple mechanisms of action to eradicate cancer

**Treatment Paradigm**
Flexible out-patient treatment strategies to drive deep responses

**Off-the-Shelf**
Stable, cryopreserved for on-demand treatment and expanded patient reach

**Uniform Products**
Consistent identity, purity and potency of cell products

**Mass Production**
Reliable manufacturing process with high yield at low cost per dose
A Novel Starting Cell Source for Cell-based Immunotherapy

Renewable clonal starting material for the generation of homogenous cell products

Human Induced Pluripotent Stem Cells (iPSCs)

*Transitioning from a heterogenous process to the cost-effective delivery of optimized cell products*

**Single-cell Derived iPSC Clone**

- Unlimited Self-Renewal
- Precise Engineering
- Uniform in Composition
- Potential to Differentiate into 200+ Cell Types
- Master Cell Banks
- Extensive Characterization

*Renewable Clonal Cell Line ---> Homogeneous Cell Products*

Fate Therapeutics’ iPSC product platform is supported by an IP portfolio of 300+ issued patents and 150+ pending patent applications
iPSC Product Platform

Disruptive Approach Enabling Mass Production of Universal NK Cell and T-Cell Products

- Multiplex engineered
- Homogeneous product
- Mass production
- Off-the-shelf

Multiple tumor-fighting mechanisms
High quality; consistent purity and activity
High yield; low cost per dose
On-demand; expanded patient reach
Creating novel multiplexed engineered iNK and iT cells with multi-antigen specificity to combat tumor heterogeneity and treatment resistance

A Snapshot of our R&D Activities

Effector function
- CD16
- CAR
- HLA knock-down
- PD-L1
- CXCR3
- IL-15RF

Resistance
- dominant negative TGF-βR

Persistence

Homing

Specificity

Multi-Antigen and Combinational Targeting of Cancer

Address: Antigen Escape, Surface Antigen Variability, Intracellular Antigens “CAR + hnCD16 + TCR + CD3/CD28

Targeting Common Tumor Tricks

Address: Stress Antigen Shedding “MICA/B”

Address: Carcinogenesis and Metastasis Signaling “B7-H3”

Address: Immune Evasion “TBA”

✓ Therapeutic mAbs
✓ Checkpoint Blockade Therapy
✓ T and NK cell engagers
✓ Radiation Therapy
✓ Multiple Immune Cells

Modified after Saetersmoen et al. Seminars in Immunopathology 2019
Best-in-Class Off-the-Shelf CAR Product Candidates With Multi-Antigen Capacity

First wave of precisely engineered CAR-mediated effector cells derived from master iPSC lines
FT596: hnCD16 + CAR19 + IL15-RF iPSC-derived NK Cell Product Candidate

Novel Dual-antigen Targeting Strategy to Overcome Tumor Heterogeneity and Antigen Escape for a Durable Response in B cell Malignancies

High-affinity Non-cleavable CD16 to Maximize ADCC

hnCD16 + 158VV High-affinity Non-cleavable mAb

Engineered IL-15 Receptor Fusion for Cytokine Support

IL-15RF Designed to promote survival, proliferation and anti-tumor activity

Engineered to be complete, consisting of both IL15 and IL15 receptor for maximum activity

CAR Optimized for NK Cell Biology

CD19-CAR anti-CD19 scFV

NK-tailored signalling tail

engineered to be complete, consisting of both IL15 and IL15 receptor for maximum activity

Stem Cell Reports 2014; Plos One 2016; Cell Stem Cell 2018; Blood 2020; Science Translational Medicine 2021; Cell Stem Cell 2021
FT596: hnCD16 + CAR19 + IL15-RF iPSC-derived NK Cell Product Candidate

Novel Dual-antigen Targeting Strategy to Overcome Tumor Heterogeneity and Antigen Escape

Clonal iPSC MCB → Mass production of uniformly-engineered, well-characterized, cryopreserved, off-the-shelf drug product enabling on-demand treatment and broad patient accessibility

The manufacturing process is robust – over 1 trillion iPSC-derived NK cells can be produced from a single vial of banked starting material which can be further increased with implementation of larger-scale processes.

Durable CAR-mediated Cytotoxicity

Leukemia xenograft NSG immunodeficient mouse model
**FT596-101**: B-Cell Lymphoma as Monotherapy and in Combination with Rituximab

*Phase 1 Study Design – Single-Dose, Single-Cycle Treatment*

- **Regimen A** – Monotherapy
  - Relapsed / refractory B-cell lymphoma
  - Eligibility allows for prior CD19-targeted CAR T-cell therapy
  - Single-dose, single-cycle dose escalation: 30M, 90M, 300M, 900M cells per dose ± mAb
  - **No mandatory hospitalization**: may be administered in outpatient setting

- **Regimen B1** – Rituximab Combination

Cyclophosphamide: 500 mg/m² IV x 3 days
Fludarabine: 30 mg/m² IV x 3 days
Rituximab: 1 dose at 375 mg/m² IV per cycle

**Diagram Details**:
- **± Rituximab**: Indicates the option of using rituximab in combination with the treatment regimen.
- **CY/FLU**: Denotes cyclophosphamide and fludarabine doses.
- **FT596**: Represents the administration of FT596.
- **DLT Assessment**: Indicates the day of dose-limiting toxicity assessment.
- **Optional Cycle 2 with FDA consent**: Indicates the possibility of an additional treatment cycle with FDA approval.
- **Post-Treatment Follow-Up**: Specifies the period for follow-up after treatment.

- **Cycle 1**
  - Days: -5, -4, -3, 1, 29
  - Disease Response

- **Post-Treatment**

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**Note**: The diagram illustrates the study design for the administration of FT596 in monotherapy and in combination with rituximab, highlighting the key phases and dosing regimens for the phase 1 study.
FT596-101: Interim Phase 1 Data
1-Dose, 1-Cycle Response Rates Inclusive of Prior Auto CAR19 T-cell Therapy

# FT596 Interim Phase 1 Data – 1 dose x 1 cycle

<table>
<thead>
<tr>
<th>Cycle 1, Day 29 Response</th>
<th>n=10 (mono)</th>
<th>n=10 (combo)</th>
<th>n=20 (total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCD I – 1 x 30M</td>
<td>1/3 (33%)</td>
<td>0 CR</td>
<td>0 CR</td>
</tr>
<tr>
<td>TCD II – 1 x 90M</td>
<td>3/4 (75%)</td>
<td>2 CR</td>
<td>2 CR</td>
</tr>
<tr>
<td>TCD III – 1 x 300M</td>
<td>3/3 (100%)</td>
<td>1 CR</td>
<td>2 CR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>≥ 90M FT596 Cells</th>
<th>n=7 (mono)</th>
<th>n=7 (combo)</th>
<th>n=14 (total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR – CD19 CAR T Naïve</td>
<td>6/6 (100%)</td>
<td>3 CR</td>
<td>2 CR</td>
</tr>
<tr>
<td>OR – Prior CD19 CAR T</td>
<td>0/1 (0%)</td>
<td>0 CR</td>
<td>2 CR</td>
</tr>
<tr>
<td>Total</td>
<td>6/7 (86%)</td>
<td>3 CR</td>
<td>4 CR</td>
</tr>
</tbody>
</table>

**Dose-dependent responses with 10 of 14 patients achieving OR (71%), with 7 achieving CR (50%), following single-dose, single-cycle treatment schedule with ≥ 90M FT596 cells**

≥ 90M FT596 Cells: n=7 (mono) OR – CD19 CAR T Naïve: 6/6 (100%) CR: 3/6 (50%) OR – Prior CD19 CAR T: 0/1 (0%) CR: 2/3 (67%) Total: 6/7 (86%) CR: 3/7 (43%)

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aCAR19 = autologous CD19-targeted CAR T-cell therapy; CR = complete response; M = million; OR = objective response; TCD = total cell dose
Interim FT596 Phase 1 results are as of June 25, 2021 data cutoff date. Response assessment for 3 patients was entered into database subsequent to data cutoff.
Interim FT596 Phase 1 results are inclusive of patients having received prior CD19-targeted CAR T-cell therapy
Day 29 protocol-defined response assessment per Lugano Classification
Summary: Prospects for Off-the-Shelf Multi-Antigen Targeting Cellular Therapy

Off-the-Shelf
(Engineered) Single Pluripotent Stem Cell
- Renewable
- Potential to differentiate into 200+ cell types

Expansion & Banking
- Master Cell Bank
  - Working Cell Banks

Differentiation & Expansion
- T Cell
- Off-the-Shelf Homogeneous | Multi-Dosing (Engineered) Cell Products
- NK Cell

Unlimited Supply of Clonal Master iPSC Lines

Thousands of Clonally-derived Doses of Cell Products

Novel Targeting Strategies
- FT596 [CAR-19]
- FT576 [CAR-BCMA]
- FT536 [CAR-MICA/B]

“to eliminate cancer”

“to reach more patients in need”
Acknowledgements

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The Fantastic People of Fate Therapeutics

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Patients, Families and Treatment Sites